

Application No. 10/779,731  
Reply to Office Action  
July 25, 2005

### REMARKS

The indication that claim 47 is free of the prior art is acknowledged with appreciation.

Non-elected claims 53-64 have been canceled without prejudice to, or disclaimer of, applicants' rights to prosecute the subject matter thereof in an appropriate divisional application.

The dependency of claim 49 has been corrected. Applicants thank the Examiner for pointing out this inadvertent clerical error in the claim.

The definite article has been substituted for the initial indefinite article in dependent claims 47-52 in accordance with the Examiner's suggestion.

The first paragraph has been amended to update the status of the parent application.

Responsive to the rejection of claim 47 under 35 U.S.C. §112, first paragraph, attention is directed to the paragraph added to page 19, line 15 of the specification by the First Preliminary Amendment filed February 18, 2004 which includes complete, updated deposit information for the deposited antibodies. Any basis for this rejection is believed to have been obviated by this amendatory matter. Withdrawal of the rejection is requested.

The rejection of claims 46 and 48-52 under 35 U.S.C. §112, first paragraph, for alleged lack of enablement is respectfully traversed. The full sequence of VEGF-D is known (see e.g. WO 98/07832, of record). It is unquestionably within the skill of the art to raise monoclonal antibodies to this known protein. Indeed, it can be done analogously to the procedure used to obtain the specifically disclosed antibodies. Should the examiner deem otherwise, he is respectfully requested to explain what difficulty a skilled worker would encounter. The determination of whether such antibodies interfere with binding between VEGF-D and VEGF receptor-3 is nothing more than a routine screening operation of the type which the Federal Circuit stated *In re Wands* did not give rise to a lack of enablement. The necessary labeling and imaging steps can also be carried out following the procedures described in detail in the specification

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using the specifically disclosed antibodies. Thus the disclosure fully enables the practice of the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

The rejection of claim 47 under 35 U.S.C. §112, second paragraph has been obviated by providing antecedent basis for the recited fragments in parent claim 46. Support for the amendment is found in claim 47. The rejection of claim 48 under 35 U.S.C. §112, second paragraph is respectfully traversed. Claim 46 is generic to all antibodies which interfere with the binding of VEGF-D to VEGF receptor-3, regardless of whether or not they are labeled with a detectable label. Claim 48 further limits claim 46 to antibodies which are labeled with a detectable label. No lack of antecedent basis is seen. Reconsideration and withdrawal of the rejections are respectfully requested.

The rejection of claims 46 and 48-51 under 35 U.S.C. §102(a) over published PCT application WO 98/07832 is respectfully traversed because the cited document does not describe the claimed invention. The cited document merely notes that antibodies to VEGF-D could be labeled with a detectable label and used for imaging. Conspicuously absent is any description of antibodies which interfere with binding of VEGF-D to VEGF receptor-3. Also missing is any description of lymphatic vasculature. Inasmuch as the cited reference fails to describe these aspects of the claimed invention it does not describe each and every feature of the claimed invention as required for a proper anticipation rejection. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

The rejection of claims 46, 48-50 and 52 under 35 U.S.C. §103(a) over WO 98/07832 and Harlow et al., Antibodies, a Laboratory Manual is also respectfully traversed. The deficiencies of the primary reference are noted above. Harlow et al. merely discloses antibody labeling with various labels such as fluorescein-5-isothiocyanate (FITC) but does not rectify the failures of the cited WO publication. Thus even if the teaching of the WO publication and Harlow et al. were combined and the antibodies of the WO publication were labeled with FITC,

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the result would still not correspond to the presently claimed invention. The combination of references thus fails to make out a proper, *prima facie* case of obviousness, and reconsideration and withdrawal of the rejection are respectfully requested.

Finally, the rejection of claims 46 and 48-52 under 35 U.S.C. §103(a) over Thorpe et al., US 6,842,219 in view of Jukov et al., EMBO J., 16(13):8898-911 (1997) is also respectfully traversed.

First, let it be noted that the Thorpe et al. patent is not prior art with respect to the present application as it was not filed until April 28, 2000, which is subsequent to the December 21, 1999 filing date of applicant's grandparent application. No showing has been made that the pertinent disclosure of Thorpe et al. was present in the April 28, 1999 provisional application from which Thorpe claims priority, and in the absence of such a showing, Thorpe et al. cannot be attributed the benefit of their provisional application. Moreover, even the date of the Thorpe et al. provisional application is subsequent to the date of applicants' December 21, 1998 provisional application. Thus, Thorpe et al. does not appear to be a proper prior art reference.

Moreover, Thorpe et al. merely discloses the use of labeled antibodies which block binding of VEGF to VEGF receptor-2 to image tumors. VEGF is distinct from VEGF-D. They are known to be expressed quite differently in the body. Similarly, VEGF receptor-2 is distinct from VEGF receptor-3. They also are distributed differently in the body. There is absolutely nothing in Thorpe's teaching of the use of labeled VEGF antibodies to image tumors that would suggest the use of labeled VEGF-D antibodies to image lymphatic vasculature. Rather, it appears that the relevance of Thorpe is motivated entirely by impermissible hindsight consideration of applicants' disclosure.

Jukov et al. discloses antibodies which bind to VEGF-C, which is a third factor distinct from both VEGF and VEGF-D. Jukov et al. contains nothing to compensate for the failure of Thorpe et al. to disclose or suggest use of labeled antibodies which interfere with binding of VEGF-D to VEGF receptor-3 to image

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the vasculature of the lymphatic system. Thus, even if Thorpe et al. were prior art, the combined teachings of these references would not make out a proper, *prima facie* case of obviousness. Therefore, reconsideration and withdrawal of this rejection are also respectfully requested.

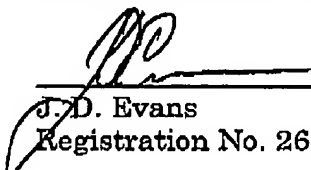
In view of the foregoing amendments and remarks, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned at (202) 624-2845 would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #029065.44660D2).

Respectfully submitted,

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